Complete Summary

GUIDELINE TITLE

Diagnosis and initial treatment of ischemic stroke.

BIBLIOGRAPHIC SOURCE(S)

Institute for Clinical Systems Improvement (ICSI). Diagnosis and initial treatment of ischemic stroke. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2007 Feb. 68 p. [135 references]

GUIDELINE STATUS

Note: This guideline has been updated. The National Guideline Clearinghouse (NGC) is working to update this summary.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s)/intervention(s) for which important revised regulatory and/or warning information has been released.

- February 28, 2008, Heparin Sodium Injection: The U.S. Food and Drug Administration (FDA) informed the public that Baxter Healthcare Corporation has voluntarily recalled all of their multi-dose and single-use vials of heparin sodium for injection and their heparin lock flush solutions. Alternate heparin manufacturers are expected to be able to increase heparin production sufficiently to supply the U.S. market. There have been reports of serious adverse events including allergic or hypersensitivity-type reactions, with symptoms of oral swelling, nausea, vomiting, sweating, shortness of breath, and cases of severe hypotension.
- <u>June 8, 2007, Troponin-I Immunoassay</u>: Class I Recall of all lots of the Architect Stat Troponin-I Immunoassay. The assay may report falsely elevated or falsely decreased results at and near a low level, which may impact patient treatment.

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **

SCOPE

METHODOLOGY - including Rating Scheme and Cost Analysis RECOMMENDATIONS

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BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

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IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT
CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

- Ischemic stroke
- Transient ischemic attack (TIA)
- Symptoms of recent neurologic dysfunction suggestive of brain ischemia

GUIDELINE CATEGORY

Diagnosis Evaluation Management Screening Treatment

CLINICAL SPECIALTY

Emergency Medicine Family Practice Internal Medicine Neurology

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Emergency Medical Technicians/Paramedics
Health Care Providers
Health Plans
Hospitals
Managed Care Organizations
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

 To increase the percentage of patients presenting within 3 hours of stroke onset who are evaluated within 10 minutes of arriving in the emergency department (ED)

- To increase the percentage of patients presenting with transient ischemic attack (TIA) symptoms within 24 hours at high risk for stroke who are admitted to the hospital
- To increase the percentage of patients receiving appropriate thrombolytic and antithrombotic therapy for ischemic stroke (use of tissue plasminogen activator [tPA] and aspirin)
- To increase the percentage of non-tPA recipients who have hypertension appropriately managed in the first 48 hours of hospitalization or until neurologically stable
- To increase the percentage of patients who receive appropriate medical management for prevention of complications within the initial 24 to 48 hours of diagnosis
- To improve patient and family education of patients with ischemic stroke in both the ED and the admitting hospital unit

TARGET POPULATION

Patients age 18 years or older with symptoms of recent neurologic dysfunction suggestive of brain ischemia

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Evaluation/Screening

- 1. Emergency department (ED) or clinic evaluation, as appropriate
- 2. History and physical examination, including neurologic examination (use of National Institutes of Health Stroke Scale [NIHSS]), risk assessment using ABCD score, and establishing time of symptom onset
- 3. Screening for tissue plasminogen activator (tPA) treatment indications and contraindications
- 4. Diagnostic testing, such as laboratory testing (e.g., complete blood count, electrolytes, blood urea nitrogen, creatinine, glucose, international normalized ratio, partial thromboplastin time, troponin, aspartate aminotransferase [AST], urine or serum pregnancy testing), electrocardiogram, computed tomography of the head without contrast, cardiac monitoring
- 5. Other cardiac assessment (telemetry) as appropriate
- 6. Considering if intra-arterial thrombolysis is appropriate

Management/Treatment

- 1. Education of patient/family regarding diagnosis, ED process, tests, treatment and risks
- 2. Blood pressure (BP) management
- 3. Measures to treat hyperthermia or hypo-/hyperglycemia
- 4. Intravenous (IV) fluids (normal saline)
- 5. tPA
- 6. Aspirin (ASA) or other antithrombotics
- 7. Post ED management
 - Hospital care in intensive care unit or acute stroke unit/cardiac monitoring
 - Physical examinations, including vital signs and neurologic checks

- BP management (monitoring and treating with easily titrated agents, such as labetalol, enalaprilat, enalapril, captopril, nitroprusside, nicardipine)
- Bleeding precautions
- Monitoring for complications of therapy
- Continued treatment of hyperthermia or hypo-/hyperglycemia
- Continued IV fluids
- Deep vein thrombosis prophylaxis with low dose heparin, low-molecular-weight heparin (e.g., enoxaparin) or heparinoids (e.g., danaparoid); intermittent pneumatic compression
- Swallow evaluation
- Early rehabilitation
- Nutritional status assessment

MAJOR OUTCOMES CONSIDERED

- Early stroke recurrence
- Stroke progression
- Mortality due to stroke
- Disability due to stroke

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

A literature search of clinical trials, meta-analysis, and systematic reviews is performed.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Key conclusions (as determined by the work group) are supported by a conclusion grading worksheet that summarizes the important studies pertaining to the conclusion. Individual studies are classed according to the system presented below, and are designated as positive, negative, or neutral to reflect the study quality.

Conclusion Grades:

Grade I: The evidence consists of results from studies of strong design for answering the question addressed. The results are both clinically important and consistent with minor exceptions at most. The results are free of any significant doubts about generalizability, bias, and flaws in research design. Studies with negative results have sufficiently large samples to have adequate statistical power.

Grade II: The evidence consists of results from studies of strong design for answering the question addressed, but there is some uncertainty attached to the conclusion because of inconsistencies among the results from the studies or because of minor doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from weaker designs for the question addressed, but the results have been confirmed in separate studies and are consistent with minor exceptions at most.

Grade III: The evidence consists of results from studies of strong design for answering the question addressed, but there is substantial uncertainty attached to the conclusion because of inconsistencies among the results of different studies or because of serious doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from a limited number of studies of weak design for answering the question addressed.

Grade Not Assignable: There is no evidence available that directly supports or refutes the conclusion.

Study Quality Designations

The quality of the primary research reports and systematic reviews are designated in the following ways on the conclusion grading worksheets:

Positive: indicates that the report or review has clearly addressed issues of inclusion/exclusion, bias, generalizability, and data collection and analysis.

Negative: indicates that these issues (inclusion/exclusion, bias, generalizability, and data collection and analysis) have not been adequately addressed.

Neutral: indicates that the report or review is neither exceptionally strong nor exceptionally weak.

Not Applicable: indicates that the report is not a primary reference or a systematic review and therefore the quality has not been assessed.

Classes of Research Reports:

A. Primary Reports of New Data Collection:

Class A:

Randomized, controlled trial

Class B:

Cohort study

Class C:

- Nonrandomized trial with concurrent or historical controls
- Case-control study
- Study of sensitivity and specificity of a diagnostic test
- Population-based descriptive study

Class D:

- Cross-sectional study
- Case series
- Case report
- B. Reports that Synthesize or Reflect upon Collections of Primary Reports:

Class M:

- Meta-analysis
- Systematic review
- Decision analysis
- Cost-effectiveness analysis

Class R:

- Consensus statement
- Consensus report
- Narrative review

Class X:

Medical opinion

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

New Guideline Development Process

A new guideline, order set, and protocol is developed by a 6- to 12-member work group that includes physicians, nurses, pharmacists, other healthcare professionals relevant to the topic, along with an Institute for Clinical Systems Improvement (ICSI) staff facilitator. Ordinarily, one of the physicians will be the leader. Most work group members are recruited from ICSI member organizations, but if there is expertise not represented by ICSI members, 1 or 2 members may be recruited from medical groups or hospitals outside of ICSI.

The work group will meet for seven to eight three-hour meetings to develop the guideline. A literature search and review is performed and the work group members, under the coordination of the ICSI staff facilitator, develop the algorithm and write the annotations and footnotes and literature citations.

Once the final draft copy of the guideline is developed, the guideline goes to the ICSI members for critical review.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Clinical Validation-Pilot Testing Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Critical Review Process

Every newly developed guideline or a guideline with significant change is sent to ICSI members for Critical Review. The purpose of critical review is to provide an opportunity for the clinicians in the member groups to review the science behind the recommendations and focus on the content of the guideline. Critical review also provides an opportunity for clinicians in each group to come to consensus on feedback they wish to give the work group and to consider changes necessary across systems in their organization to implement the guideline.

All member organizations are expected to respond to critical review guidelines. Critical review of guidelines is a criterion for continued membership within the Institute for Clinical Systems Improvement (ICSI).

After the critical review period, the guideline work group reconvenes to review the comments and make changes, as appropriate. The work group prepares a written response to all comments.

Approval

Each guideline, order set, and protocol is approved by the appropriate steering committee. There is one steering committee each for Respiratory, Cardiovascular, OB/GYN, and Preventive Services. The Committee for Evidence-based Practice approves guidelines, order sets, and protocols not associated with a particular category. The steering committees review and approve each guideline based on the following:

- Member comments have been addressed reasonably.
- There is consensus among all ICSI member organizations on the content of the document.
- Within the knowledge of the reviewer, the scientific recommendations within the document are current.
- Either a critical review has been carried out, or to the extent of the knowledge of the reviewer, the changes proposed are sufficiently familiar and sufficiently agreed upon by the users that a new round of critical review is not needed.

Once the guideline, order set, or protocol has been approved, it is posted on the ICSI Web site and released to members for use. Guidelines, order sets, and protocols are reviewed regularly and revised, if warranted.

Revision Process of Existing Guidelines

ICSI scientific documents are revised every 12 to 36 months as indicated by changes in clinical practice and literature. Every 6 months, ICSI checks with the work group to determine if there have been changes in the literature significant enough to cause the document to be revised earlier than scheduled.

Prior to the work group convening to revise the document, ICSI members are asked to review the document and submit comments. During revision, a literature search of clinical trials, meta-analysis, and systematic reviews is performed and reviewed by the work group. The work group will meet for 1-2 three-hour meetings to review the literature, respond to member organization comments, and revise the document as appropriate.

If there are changes or additions to the document that would be unfamiliar or unacceptable to member organizations, it is sent to members to review prior to going to the appropriate steering committee for approval.

Review and Comment Process

ICSI members are asked to review and submit comments for every guideline, order set, and protocol prior to the work group convening to revise the document.

The purpose of the Review and Comment process is to provide an opportunity for the clinicians in the member groups to review the science behind the recommendations and focus on the content of the order set and protocol. Review and Comment also provides an opportunity for clinicians in each group to come to consensus on feedback they wish to give the work group and to consider changes needed across systems in their organization to implement the guideline.

All member organizations are encouraged to provide feedback on order sets and protocol, however responding to Review and Comment is not a criterion for continued membership within ICSI.

After the Review and Comment period, the work group reconvenes to review the comments and make changes as appropriate. The work group prepares a written response to all comments.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note: This guideline has been updated. The National Guideline Clearinghouse (NGC) is working to update this summary. The recommendations that follow are based on the previous version of the guideline.

Note from the National Guideline Clearinghouse (NGC) and the Institute for Clinical Systems Improvement (ICSI): For a description of what has changed since the previous version of this guidance, refer to "Summary of Changes Report -- February - 2007."

The recommendations for the diagnosis and initial treatment of ischemic stroke are presented in the form of three algorithms with 38 components, accompanied by detailed annotations. Algorithms are provided for: Screening (Ambulatory), Emergency Department Treatment, and Stroke Code; clinical highlights and selected annotations (numbered to correspond with the algorithm) follow.

Class of evidence (A-D, M, R, X) and conclusion grade (I-III, Not Assignable) definitions are repeated at the end of the "Major Recommendations" field.

Clinical Highlights

- Patients presenting with signs and symptoms of transient ischemic attack (TIA) should be evaluated for risk of immediate future events using the ABCD score. (Annotation #23)
- Patients who present in time to be candidates for treatment with tissue plasminogen activator (tPA) should be evaluated by a physician within 10 minutes, undergo a computed tomography (CT) scan within 25 minutes of arrival in the emergency department (ED), and have CT interpreted within 20 minutes of test completion. (Annotations #29)
- Intravenous (IV) tPA, if given, should be administered within 3 hours of stroke onset and less than 60 minutes of arrival at the ED. (*Annotations #29, 30, 33, 37*)
- Patients presenting with stroke onset who are not candidates for IV tPA should promptly be given aspirin, after exclusion of hemorrhage on CT scan. (Annotation #37)

- Education regarding early stroke symptoms, risk factors, diagnostic procedures, and treatment options should be offered to the patient and family. This should be documented in the patient chart. (Annotation #37)
- Medical management for prevention of complications; within the initial 24 to 48 hours of diagnosis and initial treatment of ischemic stroke include: (Annotation #38)
 - Continue appropriate blood pressure management
 - Continue to treat hyperthermia
 - Continue to treat hypo- or hyperglycemia
 - Continue IV fluids
 - Initiate deep vein thrombosis prophylaxis
 - Perform swallow evaluation
 - Initiate early rehabilitation
 - Perform nutritional status assessment

Screening (Ambulatory) Algorithm Annotations

1. Initial Contact with Patient and Complaint of Neurological Symptoms

This contact may occur with one of several medical system personnel, including primary care physicians, other medical specialty physicians, emergency medical personnel, nursing staff in a clinic or urgent care setting or even non-medical triage personnel. This does not refer to the ED evaluation. This contact may be by phone or in person. Potential staff contacts should be educated in the importance of stroke symptom recognition and the appropriate triage measures that should be taken.

2. Immediate Screening for Ischemic Stroke

This should include detail as to the location, severity, duration of symptoms, and any aggravating or relieving factors. Symptoms that are commonly associated with ischemic stroke or transient ischemic attack (TIA) include:*

- Sudden numbness or weakness of the face, arm, or leg--especially on one side of the body
- Sudden mental confusion, trouble speaking or understanding
- Sudden trouble walking, dizziness, loss of balance or coordination
- Sudden trouble seeing in one or both eyes
- Sudden severe headache with no known cause

Symptoms of ischemic stroke can be represented in many different ways; further symptoms are too numerous to list.

Clinical diagnoses with neurologic symptoms that may imitate or superficially resemble ischemic stroke or TIA include the following:

Migraine

^{*} List from American Stroke Association for public education

Neurologic symptoms experienced with migraine tend to have a more gradual onset and slower development. However, the two problems may be indistinguishable.

Seizures

Although seizures typically consist of a "positive" phenomenon (jerking of a limb) rather than loss of neurologic function (weakness or paralysis of a limb), symptoms and signs during the ictus or in the postictal state may be similar to ischemic stroke (e.g., confusion or speech arrest during the ictus as in complex partial seizure, postictal confusion, postictal paralysis, and other sensory or visual phenomenon.)

Syncope

Transient global amnesia

This is characterized by a sudden onset antegrade and retrograde memory disturbance without other neurologic symptoms. If the patient experiences symptoms of transient global amnesia it would be inappropriate to assume the diagnosis without a complete neurologic exam.

Peripheral nerve disorders

Mononeuropathy and radiculopathy can be distinguished from ischemic stroke by the anatomic distribution of the symptoms and in the case of radiculopathy, by the associated painful symptoms. Bell's palsy, vestibular neuritis and extraocular muscle imbalance due to cranial neuropathy may also imitate ischemic stroke; a complete history and neurologic examination is required to accurately differentiate from ischemic stroke.

• Intracranial hemorrhage

• Other intracranial masses, (e.g., tumor, abscess [often differentiated by CT])

The mode of onset and early course tend to be more gradual in development.

Neuroses

Neuroses such as anxiety or panic disorder may need to be considered in some cases.

Metabolic disorders

Hypoglycemia is the most common metabolic disorder producing neurologic symptoms that imitate stroke. A patient with known diabetes or liver disease should be screened for hypoglycemia. This discussion is not meant to represent a detailed guide to discerning between ischemic stroke and other diagnoses. If there is any uncertainty as to symptom causation, the evaluation should proceed as though ischemic stroke or TIA is confirmed so as not to delay appropriate emergency treatment if needed.

4. Refer to ED or Physician's Office as Appropriate for Other Conditions

Some of the diagnoses outlined in Annotation #2, "Immediate Screening for Ischemic Stroke" may warrant ED evaluation because of the urgency of the problem itself or the inability of the contact person to distinguish the other condition from ischemic stroke. In these uncertain cases, the contact person should continue on to box #5 in the Screening (Ambulatory) Algorithm.

5. Symptoms Present Now?

Refers to ongoing symptoms suggestive of cerebral ischemia. If symptoms have resolved and were present for less than 24 hours, this is clinically defined as a TIA.

6. Possible Ischemic Stroke -- Symptoms Onset Within 24 Hours?

Key Point:

• The onset of symptoms should be defined as the last time the patient was known to be normal or at previous pre-stroke baseline.

If the symptoms resolve completely and then recur, for the purposes of determining whether thrombolysis can be considered for stroke, the time of onset would be the last time the patient was normal (just prior to the onset of the second set of symptoms). Patients may be unable to give this information if they have an aphasia or mental confusion. Family members or other witnesses may need to give this information. If the patient was sleeping and awoke with the problem, the time of onset would be the moment the patient was last known to be normal just before falling asleep.

7. Ischemic Stroke Symptoms Present for >24 Hours/Symptoms Mild and Stable

Patients with stable mild deficits present longer than 24 hours may be transported to the ED for evaluation and treatment by means other than 911. As a rule, they should be admitted to the hospital to assure thorough and expeditious evaluation and treatment. Outpatient evaluation and treatment is an acceptable alternative if it can be done as quickly as it could be done inpatient and if all goals of inpatient assessment (diagnosis of mechanism, initiation of appropriate secondary prevention, prevention of complications, early assessment for and deployment of rehabilitative services) can be successfully addressed.

9. Possible TIA -- Symptoms Within Two Hours?

Patients presenting with history suggestive of TIAs may have neurological deficits they are unaware of. To avoid missing the thrombolytic treatment window, patients with possible TIAs presenting within 2 hours of symptom onset should be triaged like patients with stroke.

10. TIA Symptoms >Two Hours Ago, but Within Last 24 Hours?

This work group recommends that the physician strongly consider hospitalization for TIA patients who appear in the ED within 24 hours of the event to expedite work-up and possibly administer tPA if the deficit recurs.

11. Transport to ED

Patients should be taken to the ED urgently.

12. TIA Symptoms >24 Hours Ago, but Within Last 7 Days?

Patients with a single episode of transient ischemic symptoms greater than 24 hours from presentation but within the last seven days should be considered for a rapid outpatient evaluation (TIA clinic) or hospitalization within 48 hours.

14. Rapid Outpatient Evaluation Within 48 Hours or Admit to Hospital

Patients should receive rapid outpatient evaluation (TIA Clinic) or be admitted to the hospital within 48 hours. In addition to a risk assessment for stroke, the patient should be diagnostically evaluated for:

- Carotid imaging: ultrasound, computed tomography angiography (CTA) or magnetic resonance angiogram (MRA)
- Echocardiogram (if suspect cardioembolic source)

Evidence supporting this recommendation is of class: R

Emergency Department Treatment Algorithm Annotations

18. See Stroke Code Algorithm

Key Points:

- Treatment with IV tPA should begin within 3 hours (180 minutes) of symptom onset
- Patients presenting to the ED within 150 minutes of symptom onset should be evaluated rapidly for treatment with IV tPA
- Occasionally, patients may be able to receive tPA even if they present later than 150 minutes if their work-up such as laboratory evaluation has been completed and they have other aspects such IV access in place

Patients presenting to the ED soon after the onset of symptoms may be candidates for treatment with IV tissue plasminogen activator (tPA) and will 13 of 43

therefore require a rapid evaluation and treatment initiation. Although the time window from onset of symptoms to treatment can be up to 180 minutes, the evaluation in the ED will require at least 30 minutes in most cases (CT scan of head, laboratory tests performed and results returned, IV access obtained, and neurological exam and history). The guideline committee has therefore chosen 150 minutes as a practical cutoff time for this triage decision.

There are important exceptions to this time limitations guideline for triage of the patients into the "Stroke Code" process. In certain instances, the time for evaluation may be shorter and this time limit of 150 minutes for triage to "Stroke Code" evaluation may be too conservative, and could be 165 or 170 minutes. One example would be the patient who is already in the hospital and has received the appropriate laboratory evaluation, who already has an IV access, and for whom much of the history is already known. In that case, a brief neurologic exam and rapid evaluation with CT may be the only items required prior to treatment and could theoretically be performed in 10 to 15 minutes.

Refer to the original guideline document for information on tPA tested in large, randomized, placebo-controlled clinical trials.

Evidence supporting this recommendation is of classes: A, C, D, R

21. **ED Diagnostic Evaluation**

Patients with a history suggestive of TIA should be evaluated promptly. The following diagnostic evaluations should be performed before the patient leaves the ED.

- Laboratory Tests
 - Complete blood count
 - Glucose
 - Electrolytes (sodium, potassium, chloride, CO₂)
 - Sedimentation rate (ESR)
- Electrocardiogram
- Brain Imaging
 - Magnetic resonance imaging (MRI)
 - CT

Evidence supporting this recommendation is of classes: C, R

23. High Risk for Stroke?

Key Points:

- Risk of stroke is greatest in the immediate aftermath of TIA or minor stroke.
- Features of presentation define those at highest risk.
- Hospitalization should be strongly considered for those at highest risk.

Analysis of a population-based sample of TIA episodes (n=209) yielded the ABCD score identifying those at high risk of stroke.

The elements of the scale from this derivation sample are:

A – for age	Over the age of 60 years	1 point
B – for blood	A systolic greater than 140 mm Hg or diastolic	1 point
pressure	greater than 90 mm Hg	
C – for clinical	Unilateral weakness	2
features		points
	Speech disturbance without weakness	
		1 point
	Other clinical features	
		0
-		points
D – for duration of	Symptoms lasting greater than 60 minutes	2
symptoms	Symptoms lasting 10–59 minutes	points
	Symptoms lasting 10–39 minutes	1 point
	Symptoms lasting less than 10 minutes	Pome
	symptoms labeling roos than 15 minutes	0
		points
7-day risk of stroke		
0-4 points: 0.4%		
5 points: 12.1%		
6 points: 31.4%		

Not settled is whether the assessment of those at low risk can be safely pursued at a more leisurely pace or foregone altogether.

Recent reports highlight the frequent early recurrence of symptoms of stroke and other cardiovascular events. It is not clear whether hospitalization would help to mitigate further injury by ensuring appropriate surgical intervention when needed (carotid endarterectomy) or increasing the percentage of patients receiving appropriate prophylaxis early in their course. However, it would seem prudent to admit most patients to the hospital with transient ischemic attack that occurred within 48 hours of presentation in order to expedite their evaluation and address these issues promptly, given the immediate risk of recurrence. Furthermore, hospitalization would enable timely administration of lytic therapy in the interval of greatest risk, the initial 24 to 48 hours. The factors that predict high risk of recurrence might influence decision making in this patient group. Although the data available cannot define an appropriate triage decision for all patients, this information should serve as a quide for appropriate and safe management of the patient with TIA. Certain diagnostic entities if suspected may require hospitalization for specific management even with presentation later than 24 hours from TIA occurrence (e.g., carotid or vertebral artery dissection, specific coagulopathy or arteriopathy, cerebral venous thrombosis.)

In summary, the work group recommends consideration of hospitalization for patients with first TIA within the past 24 to 48 hours to facilitate early deployment of lytic therapy, if necessary, and to expedite institution of definitive secondary prevention. For others, multiple and increasingly frequent symptoms ("crescendo TIAs") and the clinical features described above might also justify hospitalization rather than expedited ambulatory management. Whatever the strategy, speed is key. Patients managed in the outpatient setting should be fully educated about the need to return immediately if symptoms recur, to allow use of lytic therapy.

Refer to the original guideline document for additional information on risk assessment which can help identify patients at high risk of stroke.

Evidence supporting this recommendation is of classes: B, C, D, M, R

Brain Imaging

If the patient is not having symptoms at the time of presentation, a diffusion-weighted MRI (DW-MRI) is preferred, if available. At this time, a MRA of the carotids and brain can be performed.

If MRA is not available, the CT of the head would be indicated and possibly CTA of the head and neck.

Evidence supporting this recommendation is of class: C

24. Admit to Monitored Unit

Patients with TIA symptoms within 24 hours and at high risk for stroke should be admitted to a monitored unit for observation and further evaluations. Admitting patients expedites diagnostic evaluation, allows for ready access to fibrinolysis should the patient have an acute stroke, facilitates early carotid revascularization if indicated, and offers greater opportunity for risk factor modification for secondary stroke prevention.

The following diagnostic evaluations should be performed with 24 hours:

25. Carotid Imaging

- Ultrasound
- CTA
- MRA

26. **Echocardiogram (EKG)** (if cardioembolic source suspected)

Evidence supporting this recommendation is of class: R

26. Rapid Outpatient Evaluation within 48 Hours of Admit to Hospital

Patients with TIA symptoms that occurred more than 24 hours ago but within the last seven days should be evaluated with 48 hours. Organizations have started TIA clinics for the rapid evaluation of patients in the outpatient setting. Patients who cannot be evaluated rapidly as an outpatient should be

admitted to the hospital. The following diagnostic evaluations should be performed with 48 hours:

- Carotid Imaging
 - Ultrasound
 - CTA
 - MRA
- **Echocardiogram** (if cardioembolic source suspected)

Stroke Code Algorithm Annotations

29. Admit and Begin Stroke Code

Key Points:

- The "door to first physician contact" goal is 10 minutes.
- The "door to initiation of CT scan" goal is 25 minutes.
- The "door to drug" goal for thrombolytic treatment is within 60 minutes.

The guideline committee uses the term "stroke code" to refer to a process in the ED for the rapid evaluation and treatment of patients who have presented in a time frame qualifying them for thrombolytic therapy. This process may take many forms. It might include a formal "stroke team" that is called whenever a possible candidate for tPA has presented or it may include the ED staff who have been trained in the rapid evaluation and treatment of stroke victims. The general concept is one that includes the following:

- Rapid triage of patients as soon as they arrive in the ED
- Immediate initiation of phlebotomy for appropriate blood tests followed by CT scan
- First physician contact for history and exam occurring early in the ED visit. The National Institutes of Health (NIH) recommendation for timing of "door to first physician contact" for thrombolytic candidates is within 10 minutes.
- Rapid access to the best neurologic and radiologic expertise available at the individual institution for evaluation of the patient and the CT scan prior to treatment.

This may include a neurologist and neuroradiologist present at the time of treatment. Alternatively, it may be a primary care physician with expertise in stroke diagnosis and administration of tPA and a general radiologist with expertise in reviewing head CT scans. The NIH recommendation for the timing of "door to initiation of CT scan" for thrombolytic candidates is within 25 minutes.

 The goal of the stroke code should be to rapidly administer tPA in appropriately screened candidates. The NIH recommendation for the timing of "door to drug" for thrombolytic treatment is within 60 minutes.

30. Evaluation (Should Occur Concurrently with Intervention)

Key Points:

- Review tPA indications/contraindications and document whether patient is eligible.
- Perform baseline National Institutes of Health Stroke Scale (NIHSS).
- Draw blood for lab tests.
- Perform EKG.
- Perform noncontrast head CT to exclude hemorrhage.

Review History and tPA Treatment Indications and Contraindications and Baseline NIHSS

Take a complete patient history including a review of indications and contraindications for treatment with tPA. The contraindications for treatment should be considered relative contraindications.

The recommendations for treatment indications and contraindications were modified from the Institute for Clinical Systems Improvement (ICSI) Technology Assessment Work Group for tPA for Acute Ischemic Stroke. They are based upon the National Institute of Neurologic Disorders and Stroke (NINDS) study recommendations with amendments to include recommendations from clinical practice at Mayo Clinic and treatment guidelines from the Stroke Treatment in the Community study.

See ICSI technology assessment <u>Tissue-type Plasminogen Activator for Acute Ischemic Stroke</u> (TA # 28, 2005) for more information.

Evidence supporting this recommendation is of class: D

Indications for tPA

- Acute onset of focal neurologic symptoms in a defined vascular territory, consistent with ischemic stroke
- Clearly defined onset of stroke less than 3 hours prior to planned start
 of treatment; if the patient awakens with symptoms, onset is defined
 as the time of the last known baseline neurological status prior to
 retiring
- Eighteen years of age or older
- CT scan does not show evidence of intracranial hemorrhage, nonvascular lesions (e.g., brain tumor, abscess) or signs of advanced cerebral infarction such as sulcal edema, hemispheric swelling, or large areas of low attenuation consistent with extensive volume of infarcted tissue

Contraindications for tPA

Clinical Contraindications

- Clearly defined onset of stroke greater than 3 hours prior to planned start of treatment; if the patient awakens with symptoms, onset is defined as the time of the last known baseline neurological status prior to retiring
- Rapidly improving symptoms
- Mild stroke symptoms/signs (NIHSS less than 4)
 - Sensory symptoms only
 - Ataxia without other deficits
 - Dysarthria without other deficit
 - Mild motor signs (non-disabling)
 - Visual field defect without other deficit
- In the setting of middle cerebral artery (MCA) stroke, an obtunded or comatose state may be a relative contraindication.
- Seizure at onset of stroke symptoms or within the 3 hours prior to tPA administration
- Clinical presentation suggestive of subarachnoid hemorrhage regardless of CT result
- Hypertension--systolic blood pressure (SBP) greater than 185 mm Hg or diastolic blood pressure (DBP) greater than 110 mm Hg

Patients with an SBP greater than 185 mm Hg or DBP greater than 110 mm Hg are excluded only if the blood pressure remains elevated on consecutive measurements, or if aggressive treatment is required to lower the blood pressure into an appropriate range.

History Contraindications

- Minor ischemic stroke within the last month
- Major ischemic stroke or head trauma within the last three months
- History of intracerebral or subarachnoid hemorrhage if recurrence risk is substantial
- Untreated cerebral aneurysm, arteriovenous malformation (AVM), or brain tumor
- Gastrointestinal or genitourinary hemorrhage within the last 21 days
- Arterial puncture at a noncompressible site within the last seven days or lumbar puncture within the last three days
- Major surgery or major trauma within the last 14 days
- Clinical presentation suggestive of acute myocardial infarction (MI) or post-MI pericarditis
- Patient taking oral anticoagulants and international normalized ratio (INR) greater than 1.7
- Patient receiving heparin within the last 48 hours and having an elevated activated partial thromboplastin time (aPTT)
- Patient receiving low-molecular-weight heparin within the last 24 hours
- Pregnant, or anticipated pregnant, female
- Known hereditary or acquired hemorrhagic diathesis or unsupported coagulation factor deficiency

Laboratory Contraindications

Glucose should always be measured prior to giving tPA; other parameters should be checked before treatment if there is reason to believe they may be abnormal (e.g., INR and aPTT should be checked if patient has been exposed recently to warfarin or heparin or if there is history of liver disease).

- Glucose less than 50 or greater than 400 mg/dL
- Platelet count less than 100,000/mm³
- INR greater than 1.7
- Elevated aPTT
- Positive pregnancy test

Radiology Contraindications

- Intracranial hemorrhage
- Large area of low attenuation consistent with an infarcted brain

Early changes of this type suggest that onset of symptoms occurred earlier than the history first indicated. Recheck patient history and time of symptom onset.

• Intracranial tumor, aneurysm, arteriovenous malformation or other space-occupying lesion

Once indications and contraindications have been reviewed, documentation of why patient was included or excluded must occur.

Baseline NIHSS

A history and neurological examination must be performed to assess whether the presentation is consistent with a stroke diagnosis and to estimate the severity of the deficit. Use of the NIHSS by physicians and nursing staff is encouraged, as this would provide a uniform method of evaluation to facilitate comparison between examiners during the early hours of the stroke evaluation. The work group encourages use of the NIHSS as an initial evaluation tool and after resuscitation or treatment to assess for change.

The NIHSS is a quantitative measure of neurologic deficit in stroke patients that covers the key aspects of the neurological exam, including: level of consciousness and orientation, eye movements, visual fields, facial weakness, motor strength in limbs, coordination, sensation, language and comprehension of language, articulation, and neglect. It can be performed in rapid fashion (five to eight minutes), which is an important feature in this clinical setting.

It has been demonstrated in several evaluations to have both validity and reliability.

Refer to the original guideline document for more information on baseline NIHSS

Evidence supporting this recommendation is of classes: B, C, D, R

Perform Vital Signs Every 15 Minutes with Neuro Checks (Not NIHSS)

It is the standard of practice to perform a baseline NIHSS neurological assessment. For subsequent neuro checks, do not perform the full NIHSS. Performing a full NIHSS assessment every 15 minutes is often not feasible and may not be a good use of nursing time, as there is not any evidence to show performing a full NIHSS assessment every 15 minutes improves patient outcomes or improves the assessment and early detection of changes in patient condition. However, there is not a standard validated non-NIHSS neurological assessment that is utilized by health care providers or that has been studied.

The work group has gathered the abbreviated neurological assessments used by several organizations and would like to propose the following non-NIHSS neuro check as a guide.

Level of Consciousness – measures the level of alertness of the patient

- Is the patient alert, alert with stimulation or requires repeated stimulation to remain alert, or comatose?
- Is the patient able to correctly mouth his/her name and age?
- Is the patient able to correctly follow simple commands of opening and closing his/her eyes?

Motor Functions – measures the motor functions and patient's ability to follow commands

- Is the patient able to perform a series of arm movements?
- Is the patient able to perform a series of leg movements?

Language Skills – measures the amount of aphasia and dysarthria in response to asking patients to describe an item or read several sentences

See Appendix B in the original guideline document for examples of non-NIHSS neuro check forms.

The work group would like to encourage organizations to measure the use of non-NIHSS assessment tools to grow the evidence in this area.

Record Weight (Estimate If Needed)

Draw Blood for Lab Tests

Necessary/critical laboratory tests (results must be available before treatment in all cases):

- Glucose
- Prothrombin time (PT)/INR (if patient on warfarin)

Recommended laboratory tests (results must be available before treatment if physical exam and/or patient history indicates the possibility of abnormal results):

- Complete blood count (CBC) with platelet count
- Electrolytes, blood urea nitrogen (BUN), creatinine
- PT/INR, aPTT

Others to consider:

- Troponin
- Aspartate aminotransferase (AST)

These tests are used to evaluate for dehydration, metabolic disorders which might influence neurologic status (especially hypoglycemia and hyperglycemia), hematologic disorders such as polycythemia which may affect cerebral perfusion, or coagulopathies which could affect the treatment decision. Prior to administration of tPA, the platelet count and glucose level should be reviewed. If the patient is known to be on warfarin or has received heparin within the last 24 hours, the prothrombin time and partial thromboplastin time should be reviewed prior to treatment. A urine or serum pregnancy test should be obtained in women of childbearing potential if there is substantial reason to believe the patient may be pregnant.

Perform EKG

An EKG should be performed for the purpose of screening for concomitant cardiac disease, either acute or chronic which may impact on immediate treatment decisions.

Perform CT Head Without Contrast

A CT scan without contrast must be performed prior to treatment with tPA, primarily for the purpose of excluding hemorrhage. Early signs of infarct should also be sought as this finding confers greater risk of symptomatic intracerebral hemorrhage with tPA treatment. It is suggested that the greatest level of radiologic expertise possible be obtained for this reading, with the caveat that this CT reading should not create excessive delays in the evaluation and treatment process. A process for rapid teleradiography CT readings should be organized and in place if needed.

Other Cardiac Assessment as Appropriate (Telemetry)

Consider if Intra-Arterial Thrombolytic Candidate

Intra-arterial thrombolytic therapy may be a treatment option for selected patients presenting in an early time frame but beyond the three-hour time window for intravenous tPA. Please note that the management during and following intra-arterial treatment is outside the scope of this guideline.

This is not a routine treatment. The availability of this option will be institution dependent, and patients must be highly selected. If considering this treatment option for a patient, a physician must explain to the patient and family that this is an experimental treatment with substantial risk. Despite the limitations of available study data, in cases of more severe presentation with basilar artery or middle cerebral artery occlusion, intraarterial thrombolytic treatment may be appropriate because the prognosis without treatment is poor.

If the patient is an appropriate candidate for this treatment, consideration should be given to immediate transfer to an institution offering this intervention. If an endovascular interventionist skilled in this technique is available to the hospital, the patient should be mobilized quickly.

Intra-arterial infusion of a thrombolytic agent directly into a clot would have theoretic advantages over systemic (intravenous) treatment, offering a more focused approach with a purported higher recanalization rate. However, with the exception of a few small randomized controlled studies, the available evidence for intra-arterial thrombolysis primarily consists of reported case series. Consequently, if a patient can be treated within three hours, intravenous tPA should be given.

Refer to the original guideline document for emerging technologies and for information on studies investigating intra-arterial thrombolysis in patients with middle cerebral artery (MCA) and basilar artery occlusion.

31. Intervention (Should Occur Concurrently with Evaluation)

Key Points:

- Education on the suspected diagnosis of ischemic stroke and the possible treatment plans should occur with the patient and family/caregiver.
- Patients with a systolic blood pressure (SBP) greater than 185 mm Hg or diastolic blood pressure (DBP) greater than 110 mm Hg are excluded only if the blood pressure remains elevated on consecutive measurements; patients are excluded if aggressive treatment is required to lower the blood pressure into an appropriate range.
- Prevent dehydration in patients by maintaining euvolemia with isotonic fluids. Hypotonic fluids should be avoided because they promote brain swelling.
- Initiate treatment if necessary to correct hyperthermia, hypo- or hyperglycemia, and hypoxia.

Educate Patient and Family

A process should be in place for the patient and family that will rapidly orient them to the suspected diagnosis, ED process, tests to be performed, tPA treatment and its risks, and other treatment measures to be considered. This could include caregiver face-to-face interaction with the patient and family as well as teaching tools in written form. Education should be documented in the medical record.

Treat Hypertension if greater than 185 systolic and 110 diastolic

Patients with an SBP greater than 185 mm Hg or DBP greater than 110 mm Hg are excluded only if the blood pressure remains elevated on consecutive measurements; patients are excluded if aggressive treatment is required to lower the blood pressure into an appropriate range (e.g., if more than a few doses of any medication is required or if nitroprusside drip is required.)

Ischemic stroke, tPA candidate:

- No tPA if DBP is greater than 140 mm Hg on two readings, five minutes apart or use of nitroprusside is necessary to control blood pressure
- Treat SBP greater than 185 mm Hg or DBP greater than 110 mm Hg using easily titrated agents (labetalol, enalapril). Do not use tPA if BP is difficult to lower below these thresholds

Refer to the original guideline document for discussion of supporting evidence and the American Heart Association (AHA) recommendations for the management of patients with acute ischemic stroke.

In general, discontinuation of a patient's usual daily antihypertensive regimen is not advised as this may result in unwanted rebound hypertensive effects. Exceptions to this practice might include holding these medications if the BP is low and holding diuretic therapy regardless of the BP, to avoid any problems with volume depletion that might contribute to hemoconcentration that could limit blood flow.

Evidence supporting this recommendation is of classes: A, D, R

Initiate 2 IV lines

Two intravenous (IV) lines should be started so that tPA may have a dedicated line.

Start IV Fluids

Treatment with a 0.9% normal saline at a rate of 75 to 125 cc/hr or 2-3 L/day should be administered for the avoidance of dehydration. The rate may be adjusted for febrile patients.

Evidence supporting this recommendation is of classes: A, C, D, R

Treat Hyperthermia

Interventions for patients with temperatures of greater than 37.5 degrees C (99.5 degrees F) include appropriate dosing of acetaminophen (1 gram orally or 650 mg rectally every four to six hours, not to exceed 4-6 grams in 24 hours) and regular monitoring of temperature status (every four hours). For those patients with extreme hyperthermia greater than 39.4 degrees C (103 degrees F), aggressive interventions including cooling blankets and ice packs

are encouraged. Causes for temperature elevation should be sought and treated.

In human studies, early hyperthermia in acute stroke is associated with increased risk of poor outcome, higher mortality, and increased infarct volume. The causality and the relationship of temperature elevation to these poor outcomes are not fully understood. Whether intervention with cooling methods will result in improved outcomes is unknown. [Conclusion Grade III: See Conclusion Grading Worksheet A -- Annotation #31 (Hyperthermia) in the original guideline document]

Evidence supporting this recommendation is of classes: B, D, M, R

Treat Hyperglycemia

Hyperglycemia may adversely influence clinical outcome.

- Early identification of patients with hyperglycemia in the setting of acute ischemic stroke or in those at risk for cerebral ischemia (ED evaluation of glucose level) is recommended.
- Avoid any agents or factors which might induce hyperglycemia.
 - Eliminate glucose from any IV solutions used. (Recommend use of normal saline.)
 - Avoid use of corticosteroids, even in those patients with cerebral edema, as they are not helpful and may be harmful.
 Separate recommendations are needed for those on maintenance corticosteroids, for concurrent conditions, and treatment decisions are left to the discretion of the physician.
 - Use appropriate measures to maintain euglycemia, carefully avoiding hypoglycemia.
 - Continue to monitor glucose with bedside testing in those receiving treatment in order to maintain euglycemia.

It is unclear whether early hyperglycemia in the setting of acute stroke may be a marker of physiologic stress or an independent predictor of poor outcome. Usual management of hyperglycemia with gentle dosing of subcutaneous insulin in a timely manner during acute ischemia would seem prudent until ongoing clinical trials address the appropriateness of more aggressive treatment measures. [Conclusion Grade III: See Conclusion Grading Worksheet B - Annotation #31(Hyperglycemia) in the original quideline document]

Evidence supporting this recommendation is of classes: A, B

32. Patient Meets Criteria for tPA, Has No Contraindications and Symptom Onset Still Less Than Three Hours?

Refer to Algorithm Annotation #30, "Evaluation (Should Occur Concurrently With Intervention)," for criteria.

33. Initiate tPA

Treatment should consist of tPA 0.9 mg/kg intravenously to a maximum dose of 90 mg. Ten percent of this dose should be given as a bolus over one to two minutes and the remainder infused over one hour. This dosing may be based upon actual or estimated weight.

35. Initiate Aspirin Unless Contraindicated

Key Points:

- Aspirin should be given rectally or via nasogastric (NG) tube promptly in patients who are not rt-PA candidates unless contraindicated (aspirin allergy, gastrointestinal [GI] bleeding).
- There is no evidence to support therapeutic anticoagulation with unfractionated heparin, low-molecular weight (LMW) heparin or heparinoids. There is, as yet, insufficient evidence to decide whether specific subgroups of ischemic stroke (e.g., dissection, cardioembolism with intra-cardiac clot) will benefit from therapeutic anticoagulation.
- If a decision is made to use continuous heparin infusion, boluses should be avoided and aPTT should be maintained in the 1.5–2 times baseline range.
- Low dose prophylactic anticoagulation (e.g., unfractionated heparin 5,000 units subcutaneously twice daily) is beneficial for prevention of deep vein thrombosis (DVT) or pulmonary embolism (PE) in stroke patients with limited mobility.

Aspirin

Patients who are not candidates for tPA should be promptly given aspirin in a dose of 160 to 325 mg orally, rectally, or by nasogastric tube and should be continued on a similar daily dose. Exceptions to this approach would include avoiding treatment in those with contraindications to aspirin therapy (e.g., aspirin allergy, gastrointestinal hemorrhage). For patients with an aspirin allergy, 75 mg of clopidogrel may be reasonable.

Initiation of aspirin therapy should be withheld for 24 hours for patients who have received tPA.

Patients who take nonsteroidal anti-inflammatory medication (NSAIDs) for other conditions should be instructed to withhold taking NSAIDs for at least 30 minutes after taking their aspirin medication.

On September 8, 2006, the Food and Drug Administration issued a Safety Information and Adverse Event Report regarding the concomitant use of low-dose aspirin (for cardioprotective benefits) and ibuprofen.

The report indicates that 400 mg ibuprofen taken with immediate-release low-dose aspirin (81 mg) will interfere with the antiplatelet effect of aspirin. Other over-the-counter NSAIDs should be viewed as having potential to interfere with the antiplatelet effect of aspirin.

Recommendations include taking immediate release low-dose aspirin 30 minutes prior to taking ibuprofen. If ibuprofen is taken first, aspirin should not be taken for at least eight hours after ingestion of ibuprofen. Other analgesics that do not interfere with the antiplatelet effect of aspirin should be considered in populations at high-risk for cardiovascular events.

Enteric-coated aspirin and concomitant use of ibuprofen is unclear. One study showed that 400 mg ibuprofen interfered with the antiplatelet effect of enteric-coated low-dose aspirin at 2, 7 and 12 hours after ingestion.

For more information, please refer to the information listed on the Food and Drug Administration's Web site for a complete copy of the alert and cited references: http://www.fda.gov/medwatch/safety/2006/safety06.htm#aspirin

Evidence supporting this recommendation is of classes: A, C, M

Considerations with Heparin Use

Results from the International Stroke Trial provide powerful evidence against the routine use in patients with acute ischemic stroke, of any heparin regimen as intensive as the moderate dose subcutaneous regimen utilized in this very large clinical trial (unfractionated heparin - 12,500 units subcutaneous twice daily).

This would include the adjusted dose, continuous infusion of unfractionated heparin. The commonly cited indication of vertebrobasilar distribution ischemia or ischemic stroke in the setting of atrial fibrillation was analyzed separately and there was no measurable benefit in these specific subgroups. Similarly, the weight of available data regarding use of full dose low-molecular-weight heparin for the acute treatment of stroke do not support their routine use for limiting disability or decreasing mortality in this setting.

The routine use of acute anticoagulation treatment with unfractionated heparin, low-molecular-weight heparin, or heparinoid in acute ischemic stroke is not supported by the available evidence. This treatment does not appear to improve clinical outcome from the index stroke. There may be subgroups who benefit, but further studies of this problem are required for confirmation. [Conclusion Grade I: See Conclusion Grading Worksheet C- - Annotation #35 (Heparin) in the original guideline document]

Despite these discouraging results, the use of continuous heparin infusion in acute stroke has continued to be common in clinical practice. Given these data, if the decision is made to use full dose continuous heparin infusion for a specific indication (e.g., large vessel atherothrombosis or dissection), physicians are strongly encouraged to discuss with their patients the lack of proof for this therapy and to detail the potential hazards.

Heparin Use for Venous Thromboembolism (VTE) Prophylaxis

Lower doses of these agents, (e.g., enoxaparin 40 mg subcutaneously daily or unfractionated heparin 5,000 units subcutaneously twice daily), are beneficial

for the prevention of deep vein thrombosis or pulmonary embolus in those stroke victims with limited mobility and can be advocated for that purpose. Pharmacologic prophylaxis should be considered for patients at high risk for VTE, including an estimated length of stay of four days or more.

For patients of high risk for VTE where pharmacologic prophylaxis is contraindicated, elastic stockings are recommended and intermittent pneumatic compression (IPC) should be used if confined to bed.

See the NGC summary of ICSI's guideline <u>Venous Thromboembolism</u> Prophylaxis for more information.

Evidence supporting this recommendation is of classes: A, M, R

36. Post-ED Medical Management (Post-Thrombolysis)

- **Admit** to intensive care unit or acute stroke care unit/cardiac monitoring.
- **Perform vital signs and neurologic checks** (not NIHSS) every 15 minutes for 2 hours, then every 30 minutes for 6 hours, then every 60 minutes for 24 hours (recommend use of an abbreviated NIHSS for neurologic checks).
- Treat BP if greater than 180/105
 - First 24 hours: Treat if SBP greater than 180 mm Hg or DBP greater than 105 mm Hg.
 - Greater than 24 hours: Treat if SBP greater than 220 mm Hg, mean arterial pressure (MAP) greater than 130 mm Hg.
 - Monitor BP and any corresponding neurologic changes in the ED and first few days of hospitalization

• Initiate bleeding precautions:

- Avoid placement of central venous access or arterial puncture for the first 24 hours.
- Placement of an indwelling bladder catheter should be avoided during drug infusion and for at least 30 minutes after infusion ends.
- Insertion of a nasogastric tube should be avoided, if possible, during the first 24 hours.
- Avoid use of anticoagulant, antiplatelet, or non-steroidal antiinflammatory agents for the first 24 hours.
- Monitor for central nervous system (CNS) hemorrhage
- If any signs of CNS hemorrhage (e.g., neurologic deterioration, development of severe headache, sudden severe elevation of BP, or new nausea or vomiting) or signs of major systemic hemorrhage institute the following measures:
 - Discontinue infusion of thrombolytic drug.
 - Obtain hemoglobin, hematocrit, partial thromboplastin time, prothrombin time/INR, platelet count, fibrinogen (also type and cross match if transfusions will be needed).
 - Obtain surgical consultation if necessary.
 - Obtain emergent CT head without contrast if central nervous system hemorrhage suspected.
- **Initiate antithrombotic therapy** 24 hours after tPA administration (antiplatelet agent or anticoagulant as appropriate).

37. Post-ED Medical Management (Not a Thrombolysis Candidate)

Treat BP if greater than 220/120 mm Hg or MAP greater than 130 mm Hg

Recommendations - Ischemic stroke, **not** a tPA candidate:

- Treat BP only if SBP greater than 220 mm Hg, MAP greater than 130 mm Hg.
- Use easily titrated agents, choosing those with the least effect on cerebrovasculature (labetalol, enalaprilat). American Heart Association (AHA) recommendations support oral dosing, but if swallowing is affected IV agents should be used.

Note: Dosing examples are included in the original guideline document.

- Avoid agents which tend to cause precipitous drops in BP (e.g., sublingual calcium channel blockers).
- Treat hypotension (IV fluids; treat congestive heart failure or arrhythmia and consider pressors).
- Monitor BP and any corresponding neurologic changes in the ED and first few days of hospitalization. Avoid overtreating BP.

It is important to recognize that these recommendations must be tailored to the individual, dependent on the patient's acute presentation and whether or not there is a previous history of hypertension. Young patients without a previous history of hypertension may be less tolerant of the higher extremes of BP in this setting. Specific comorbidities that may require a more aggressive use of antihypertensive therapy in this setting include:

- Left ventricular failure
- Aortic dissection
- Acute myocardial ischemia
- Renal insufficiency induced by accelerated hypertension
- Hypertensive encephalopathy
- Hemorrhagic conversion of an ischemic infarct
- Thrombolytic treatment

In general, discontinuation of a patient's usual daily antihypertensive regimen is not advised as this may result in unwanted rebound hypertensive effects. Exceptions to this practice might include holding these medications if the BP is low and holding diuretic therapy regardless of the BP, to avoid any problems with volume depletion that might contribute to hemoconcentration that could limit blood flow.

38. Other Post-ED Medical Management (First 24-48 Hours)

Continue to Treat Hyperthermia, Hyperglycemia, or Hypoglycemia

Refer to Annotation #31, "Intervention (Should Occur Concurrently with Evaluation"), above.

Initiate DVT Prophylaxis

Consider DVT prophylaxis in any patient admitted to the hospital with weakness related to an ischemic stroke. The risk of DVT is high (25% to 50%), and prophylaxis with subcutaneous heparin decreases the incidence (10% to 20%). The risk of pulmonary embolism appears to be decreased as well, although numbers have been small and statistical significance not achieved.

All patients should receive patient education that includes signs and symptoms of VTE and therapy options and encouraged to ambulate early and perform flexion/extension exercises. Elastic stockings should be used for patients at high risk for VTE. Intermittent pneumatic compression should be considered for patients at high risk for VTE who have contraindications to pharmacologic prophylaxis.

Unfractionated heparin at 5,000 units every 12 hours is the standard dose; 5,000 units every 8 hours has been used in larger individuals. Low-molecular-weight heparin and heparinoids may be slightly more effective for DVT prophylaxis (decreased incidence from 22% with heparin to 13% with enoxaparin or danaparoid), and theoretically safer (less risk of bleeding), although improved safety has not been conclusively demonstrated in studies.

Low-molecular-weight heparin is renally cleared. For patients with a creatinine clearance (CrCl) less than 30 mL/min, use unfractionated heparin. The patient should be monitored for the possible development of heparin-induced thrombocytopenia (HIT) and bleeding. Obtain a platelet count and hemoglobin every other day beginning on the second day of heparin therapy.

See the NGC summary of the ICSI's guidelines <u>Antithrombotic Therapy</u> Supplement and Venous Thromboembolism Prophylaxis.

Evidence supporting this recommendation is of class: B, M, R

Perform Swallow Evaluation

Early evaluation of swallow should be performed in patients at risk of aspiration so that an appropriate diet adjustment may be instituted. Patients at risk include those with facial weakness, significant dysarthria, excessive drooling, sputtering, choking, gurgling, wet voice, or pocketing food in mouth. Clear liquids by mouth and in some cases any food or fluid should be avoided in this setting until a swallow evaluation has established the patient's level of risk for aspiration with the various consistencies.

Swallow evaluation, and dietary adjustments based on this information, and early mobilization as effective treatments for prevention of medical complications have not been adequately evaluated in randomized clinical trials. Because these interventions are safe and have a reasonable probability of improving care by decreasing complications, it is reasonable to advocate their use in this setting despite absence of proof of efficacy. Several previously published guidelines advocate these practices.

Initiate Rehabilitation Early

Early mobilization within 48 hours of admission in the form of early initiation of appropriate rehabilitation swivels or other nursing intervention is advocated for the purpose of preventing complications related to immobility including deep vein thrombosis, contractures, joint disorders, and pressure sores/decubitus ulcers.

Evidence supporting this recommendation is of class: R

Perform Nutritional Status Assessment

Assessment of the patient's baseline nutritional status and the implementation of treatments to correct any major nutritional problems are recommended. Poor nutritional status in patients admitted for stroke is associated with increased morbidity and mortality. Trials are currently underway to assess whether more intensive nutritional interventions improve outcomes for patients after stroke.

Evidence supporting this recommendation is of class: R

Definitions:

Conclusion Grades:

Grade I: The evidence consists of results from studies of strong design for answering the question addressed. The results are both clinically important and consistent with minor exceptions at most. The results are free of significant doubts about generalizability, bias, and flaws in research design. Studies with negative results have sufficiently large samples to have adequate statistical power.

Grade II: The evidence consists of results from studies of strong design for answering the question addressed, but there is some uncertainty attached to the conclusion because of inconsistencies among the results from the studies or because of minor doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from weaker designs for the question addressed, but the results have been confirmed in separate studies and are consistent with minor exceptions at most.

Grade III: The evidence consists of results from studies of strong design for answering the question addressed, but there is substantial uncertainty attached to the conclusion because of inconsistencies among the results from different studies or because of serious doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from a limited number of studies of weak design for answering the question addressed.

Grade Not Assignable: There is no evidence available that directly supports or refutes the conclusion.

Classes of Research Reports:

A. Primary Reports of New Data Collection:

Class A:

• Randomized, controlled trial

Class B:

Cohort study

Class C:

- Nonrandomized trial with concurrent or historical controls
- Case-control study
- Study of sensitivity and specificity of a diagnostic test
- Population-based descriptive study

Class D:

- Cross-sectional study
- Case series
- Case report
- B. Reports that Synthesize or Reflect upon Collections of Primary Reports:

Class M:

- Meta-analysis
- Systematic review
- Decision analysis
- Cost-effectiveness analysis

Class R:

- Consensus statement
- Consensus report
- Narrative review

Class X:

Medical opinion

CLINICAL ALGORITHM(S)

Detailed and annotated clinical algorithms are provided for:

- <u>Screening (Ambulatory)</u>
- Emergency Department Treatment

Stroke Code

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is classified for selected recommendations (see "Major Recommendations").

In addition, key conclusions contained in the Work Group's algorithm are supported by a grading worksheet that summarizes the important studies pertaining to the conclusion. The type and quality of the evidence supporting these key recommendations (i.e., choice among alternative therapeutic approaches) is graded for each study.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate screening and referral for patients presenting with neurological symptoms
- Rapid evaluation and treatment of patients who are candidates for thrombolytic therapy
- Improved management of ischemic stroke
- Effective prevention of stroke progression/recurrence
- Decreased mortality and morbidity associated with ischemic stroke

POTENTIAL HARMS

- Adverse effects of thrombolytic drugs can include signs of central nervous system hemorrhage (e.g., neurologic deterioration, development of severe headache, sudden severe elevation of blood pressure, or new nausea or vomiting) or signs of major systemic hemorrhage.
- Concomitant use of immediate-release low-dose aspirin (81 mg) and ibuprofen (400 mg) will interfere with the antiplatelet effect of aspirin.

CONTRAINDICATIONS

CONTRAINDICATIONS

Contraindications for Tissue Plasminogen Activator (tPA)

Clinical Contraindications

- Clearly defined onset of stroke greater than 3 hours prior to planned start of treatment; if the patient awakens with symptoms, onset is defined as the time of the last known baseline neurological status prior to retiring
- Rapidly improving symptoms

- Mild stroke symptoms/signs (National Institutes of Health Stroke Scale less than 4): sensory symptoms only, ataxia without other deficits, dysarthria without other deficits, mild motor signs (non-disabling), and visual field defect without other deficit
- In the setting of middle cerebral artery (MCA) stroke, an obtunded or comatose state may be a relative contraindication.
- Seizure at onset of stroke symptoms or within the three hours prior to tPA administration
- Clinical presentation suggestive of subarachnoid hemorrhage regardless of computed tomography result
- Hypertension--systolic blood pressure (SBP) greater than 185 mm Hg or diastolic blood pressure (DBP) greater than 110 mm Hg. Patients with a systolic blood pressure greater than 185 mmHg or diastolic blood pressure greater than 110 mmHg are excluded only if the blood pressure remains elevated on consecutive measurements, or if aggressive treatment is required to lower the blood pressure into an appropriate range.

History Contraindications

- Minor ischemic stroke within the last month
- Major ischemic stroke or head trauma within the last three months
- History of intracerebral or subarachnoid hemorrhage if recurrence risk is substantial
- Untreated cerebral aneurysm, arteriovenous malformation (AVM), or brain tumor
- Gastrointestinal or genitourinary hemorrhage within the last 21 days
- Arterial puncture at a noncompressible site within the last 7 days or lumbar puncture within the last three days
- Major surgery or major trauma within the last 14 days
- Clinical presentation suggestive of acute myocardial infarction (MI) or postmyocardial infarction pericarditis
- Patient taking oral anticoagulants and international normalized ratio (INR) greater than 1.7
- Patient receiving heparin within the last 48 hours and having an elevated activated partial thromboplastin time (aPTT)
- Patient receiving low-molecular-weight heparin within the last 24 hours
- Pregnant, or anticipated pregnant, female
- Known hereditary or acquired hemorrhagic diathesis or unsupported coagulation factor deficiency

Laboratory Contraindications

- Glucose less than 50 or greater than 400 mg/dL
- Platelet count less than 100,000/mm³
- INR greater than 1.7
- Elevated activated partial thromboplastin time (aPTT)
- Positive pregnancy test

Radiology Contraindications

- Intracranial hemorrhage
- Large area of low attenuation consistent with an infarcted brain

Early changes of this type suggest that onset of symptoms occurred earlier than the history first indicated. Recheck patient history and time of symptom onset.

• Intracranial tumor, aneurysm, arteriovenous malformation (AVM) or other space-occupying lesion

Contraindications to Aspirin (ASA) Therapy

- Aspirin allergy
- Gastrointestinal hemorrhage

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- These clinical guidelines are designed to assist clinicians by providing an analytical framework for the evaluation and treatment of patients, and are not intended either to replace a clinician's judgment or to establish a protocol for all patients with a particular condition. A guideline will rarely establish the only approach to a problem.
- This clinical guideline should not be construed as medical advice or medical opinion related to any specific facts or circumstances. Patients are urged to consult a health care professional regarding their own situation and any specific medical questions they may have.
- **Hyperthermia**. In human studies, early hyperthermia in acute stroke is associated with increased risk of poor outcome, high mortality, and increased infarct volume. The causality and the relationship of temperature elevation to these poor outcomes is not fully understood. Whether intervention with cooling methods will result in improved outcomes is unknown.
- **Hyperglycemia**. It is unclear whether early hyperglycemia in the setting of acute stroke may be a marker of physiologic stress or an independent predictor of poor outcome. Usual management of hyperglycemia with gentle dosing of subcutaneous insulin in a timely manner during acute ischemia would seem prudent until ongoing clinical trials address the appropriateness of more aggressive treatment measures.
- **Heparin**. The routine use of acute anticoagulation treatment with unfractionated heparin or low-molecular-weight heparin in acute ischemic stroke is not supported by the available evidence. This treatment does not appear to improve clinical outcome from the index stroke. There may be subgroups who benefit, but further studies of this problem are required for confirmation.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Once a guideline is approved for release, a member group can choose to concentrate on the implementation of that guideline. An action group is formed when a topic is selected as an initiative. In addition to the action group goals and measures, each medical group sets specific goals they plan to achieve in

improving patient care based on the particular guideline(s). Each medical group shares its experiences and supporting measurement results within the action group. This sharing facilitates a collaborative learning environment. Action group learnings are also documented and shared with interested medical groups within the collaborative.

Currently, action groups may focus on one guideline or a set of guidelines such as hypertension, lipid treatment, and tobacco cessation.

The following aims were identified by the guideline work group as key areas in which medical groups may receive benefits in implementing this guideline.

Priority Aims and Suggested Measures

1. Increase the percentage of patients presenting within three hours of stroke onset who are evaluated within 10 minutes of arriving in the emergency department (ED).

Possible measure for accomplishing this aim:

- a. Percentage of patients presenting within three hours of stroke onset who are evaluated with 10 minutes of arriving in the ED.
- 2. Increase the percentage of patients presenting with transient ischemic attack (TIA) symptoms within 24 hours at high risk for stroke who are admitted to the hospital.

Possible measure for accomplishing this aim:

- a. Percentage of patients admitted who have documentation of TIA symptoms within the last 24 hours.
- 3. Increase the percentage of patients receiving appropriate thrombolytic and antithrombotic therapy for ischemic stroke (use of tissue plasminogen activator [tPA] and aspirin).

Possible measures for accomplishing this aim:

- a. Percentage of eligible patients presenting with ischemic stroke treated with tPA.
- b. Percentage of patients who are not candidates for tPA treatment who receive aspirin within 24 hours of hospitalization, after a negative head computed tomography (CT) scan, unless contraindicated.
- c. Percentage of patients receiving tPA who are treated according to quideline (refer to Annotations #29 and 32)
- d. Percentage of patients who are candidates for tPA with a "door to drug" time (time of arrival to time of drug administration) of less than 60 minutes.
- e. Percentage of patients who undergo a CT scan within 25 minutes of arrival in the ED.
- 4. Increase the percentage of non-tPA recipients who have hypertension appropriately managed in the first 48 hours of hospitalization or until neurologically stable.

Possible measure for accomplishing this aim:

- a. Percentage of non-tPA recipients who have hypertension appropriately managed according to the guideline (refer to Annotation #33).
- 5. Increase the percentage of patients who receive appropriate medical management for prevention of complications within the initial 24 to 48 hours of diagnosis including:
 - Continue to treat hypoglycemia or hyperglycemia
 - Continue to treat hyperthermia
 - Continue intravenous (IV) fluids
 - Continue to treat hypoxia
 - Initiate deep vein thrombosis prophylaxis
 - Perform swallow evaluation
 - Initiate early rehabilitation (early mobilization)
 - Perform nutritional status assessment

Possible measures for accomplishing this aim:

- a. Percentage of patients who receive appropriate intervention for hypoglycemia and hyperglycemia.
- b. Percentage of patients who receive appropriate intervention for hyperthermia
- c. Percentage of patients who receive IV fluids
- d. Percentage of patients who receive appropriate treatment for hypoxia
- e. Percentage of patients with ischemic stroke with paralysis or other reason for immobility receiving appropriate prevention for venous thromboembolism (subcutaneous heparin or pneumatic compression device)
- f. Percentage of patients who are at risk for aspiration who receive an early swallow evaluation
- g. Percentage of patients mobilized from bed within 48 hours of admission
- 6. Improve patient and family education of patients with ischemic stroke in both the ED and the admitting hospital unit.

Possible measures for accomplishing this aim:

- a. Percentage of patients presenting in the ED with ischemic stroke onset for whom patient/family education is documented in the medical record.
- b. Percentage of patients admitted to a hospital unit with ischemic stroke for whom patient/family education is documented in the medical record.

At this point in development for this guideline, there are no specifications written for possible measures listed above. The Institute for Clinical Systems Improvement (ICSI) will seek input from the medical groups on what measures are of most use as they implement the guideline. In a future revision of the guideline, one or two measurement specifications may be included.

The following system changes were identified by the guideline work group as key strategies for health care systems to incorporate in support of the implementation of this guideline.

- Hospitals should consider developing and implementing critical pathways, standing orders and a stroke process to accomplish rapid evaluation and treatment.
 - a. Established process for expediting the evaluation and treatment of patients who are candidates for intravenous tPA
 - b. Presence of standing orders for acute stroke to include:
 - Ongoing antithrombotic therapy
 - Management of blood pressure
 - Early mobilization
 - Use of appropriate anti-embolism treatment in the paralyzed patient
- 2. A process should be in place for the patient and family that will rapidly orient them to the suspected diagnosis, ED process, tests to be performed, tPA treatment and its risks, and other treatment measures to be considered. This could include both caregiver face-to-face interactions with the patient and family as well as teaching tools in written form.

System Improvement

A recent study (*California Acute Stroke Pilot Registry [CASPR] Investigators*, 2005) analyzed the potential yield of various system improvements in increasing the percentage of ischemic stroke patients receiving intravenous tPA. The prevailing rate of tPA treatment in the study hospitals was 4.3%. The investigators modeled the effect of several interventions: patient education to call 911 immediately, optimizing emergency medical system (EMS) response, optimizing hospital systems, extending the time window of treatment. They found that patient education with immediate use of 911 would have the largest impact, increasing those treated from 4.3% to 28.6%. Next most impact was improving in-hospital systems, which would raise rate from 4.3% to 11.5%. EMS response improvements and extending the time window would be less impact (from 4.3% to 5.5% and 8.3% treated, respectively) in the hospitals studied.

Joint Commission for Accreditation of Healthcare Organizations (JCAHO) Primary Stroke Center Certification

JCAHO offers certification as Primary Stroke Centers to hospitals that meet specific qualifications. The emphasis of the process is on the early recognition and management of stroke and the scope of accreditation includes integrated efforts in public awareness, emergency medical services, emergency room and hospitalization. The link is:

http://www.jcaho.org/dscc/dsc/performance+measures/stroke+measure+set.htm

Refer to the original guideline document for information regarding the requirements for certification.

IMPLEMENTATION TOOLS

Clinical Algorithm
Pocket Guide/Reference Cards

For information about <u>availability</u>, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness Patient-centeredness Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Institute for Clinical Systems Improvement (ICSI). Diagnosis and initial treatment of ischemic stroke. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2007 Feb. 68 p. [135 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

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GUIDELINE DEVELOPER(S)

Institute for Clinical Systems Improvement - Private Nonprofit Organization

GUIDELINE DEVELOPER COMMENT

Organizations participating in the Institute for Clinical Systems Improvement (ICSI): Affiliated Community Medical Centers, Allina Medical Clinic, Altru Health System, Aspen Medical Group, Avera Health, CentraCare, Columbia Park Medical Group, Community-University Health Care Center, Dakota Clinic, ENT Specialty Care, Fairview Health Services, Family HealthServices Minnesota, Family Practice Medical Center, Gateway Family Health Clinic, Gillette Children's Specialty Healthcare, Grand Itasca Clinic and Hospital, HealthEast Care System, HealthPartners Central Minnesota Clinics, HealthPartners Medical Group and Clinics, Hutchinson Area Health Care, Hutchinson Medical Center, Lakeview Clinic,

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GUIDELINE COMMITTEE

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In the interest of full disclosure, Institute for Clinical Systems Improvement (ICSI) has adopted a policy of revealing relationships work group members have with companies that sell products or services that are relevant to this guideline topic. The reader should not assume that these financial interests will have an adverse impact on the content of the guideline, but they are noted here to fully inform readers. Readers of the guideline may assume that only work group members listed below have potential conflict of interest to disclose.

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GUIDELINE STATUS

Note: This guideline has been updated. The National Guideline Clearinghouse (NGC) is working to update this summary.

GUIDELINE AVAILABILITY

Electronic copies of the updated guideline: Available from the <u>Institute for Clinical</u> Systems Improvement (ICSI) Web site.

Print copies: Available from ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; Web site: www.icsi.org; e-mail: icsi.info@icsi.org.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Diagnosis and initial treatment of ischemic stroke. Executive summary.
 Bloomington (MN): Institute for Clinical Systems Improvement, 2007 Feb. 1
 p. Electronic copies: Available from the <u>Institute for Clinical Systems</u>
 Improvement (ICSI) Web site.
- ICSI pocket guidelines. April 2006 edition. Bloomington (MN): Institute for Clinical Systems Improvement, 2006. 298 p.

Print copies: Available from ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; Web site: www.icsi.org; e-mail: icsi.info@icsi.org.

PATIENT RESOURCES

None available

NGC STATUS

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